COMPUTER APPLICATIONS IN PHARMACEUTICAL RESEARCH AND DEVELOPMENT

SEAN EKINS, M.SC., PH.D., D.SC.

WILEY-INTERSCIENCE
A JOHN WILEY & SONS, INC., PUBLICATION

CONTENTS

PREFACE xi

ACKNOWLEDGMENTS xiii

CONTRIBUTORS xv

PART I: COMPUTERS IN PHARMACEUTICAL RESEARCH AND DEVELOPMENT: A GENERAL OVERVIEW 1

1. **History of Computers in Pharmaceutical Research and Development: A Narrative** 3
   Donald B. Boyd and Max M. Marsh
2. **Computers as Data Analysis and Data Management Tools in Preclinical Development** 51
   Weiyong Li and Kenneth Banks
3. **Statistical Modeling in Pharmaceutical Research and Development** 67
   Andrea de Gaetano, Simona Panunzi, Benoit Beck, and Bruno Boulanger

PART II: UNDERSTANDING DISEASES: MINING COMPLEX SYSTEMS FOR KNOWLEDGE 103

4. **Drug Discovery from Historic Herbal Texts** 105
   Eric J. Buenz

5. **Contextualizing the Impact of Bioinformatics on Preclinical Drug and Vaccine Discovery** 121
Darren R. Flower

6. **Systems Approaches for Pharmaceutical Research and Development** 139
Sean Ekins and Craig N. Giroux

PART III: SCIENTIFIC INFORMATION HANDLING AND ENHANCING PRODUCTIVITY 167

7. **Information Management—Biodata in Life Sciences** 169
Richard K. Scott and Anthony Parsons

8. **Chemoinformatics Techniques for Processing Chemical Structure Databases** 187
Valerie J. Gillet and Peter Willett

9. **Electronic Laboratory Notebooks** 209
Alfred Nehme and Robert A. Scoffin

10. **Strategies for Using Information Effectively in Early-Stage Drug Discovery** 229
David J. Wild

11. **Improving the Pharmaceutical R&D Process: How Simulation Can Support Management Decision Making** 247
Andrew Chadwick, Jonathan Moore, Maggie A.Z. Hupcey, and Robin Purshouse

PART IV: COMPUTERS IN DRUG DISCOVERY 275

12. **Computers and Protein Crystallography** 277
David J. Edwards and Roderick E. Hubbard

13. **Computers, Cheminformatics, and the Medicinal Chemist** 301
Weifan Zheng and Michael Jones

14. **The Challenges of Making Useful Protein-Ligand Free Energy Predictions for Drug Discovery** 321
Jun Shimada

15. **Computer Algorithms for Selecting Molecule Libraries for Synthesis** 353
Konstantin V. Balakin, Nikolay P. Savchuk, and Alex Kiselyov

16. **Success Stories of Computer-Aided Design** 377
Hugo Kubinyi

17. Pharmaceutical Research and Development Productivity: Can Software Help? 425
Christophe G. Lambert and S. Stanley Young

PART V: COMPUTERS IN PRECLINICAL DEVELOPMENT 443

18. Computer Methods for Predicting Drug Metabolism 445
Sean Ekins

19. Computers in Toxicology and Risk Assessment 469
John C. Dearden

20. Computational Modeling of Drug Disposition 495
Cheng Chang and Peter W. Swaan

21. Computer Simulations in Pharmacokinetics and Pharmacodynamics: Rediscovering Systems Physiology in the 21st Century 513
Paolo Vicini

22. Predictive Models for Better Decisions: From Understanding Physiology to Optimizing Trial Design 529
James R. Bosley, Jr.

PART VI: COMPUTERS IN DEVELOPMENT DECISION MAKING, ECONOMICS, AND MARKET ANALYSIS 555

23. Making Pharmaceutical Development More Efficient 557
Michael Rosenberg and Richard Farris

24. Use of Interactive Software in Medical Decision Making 571
Renée J. Goldberg Arnold

PART VII: COMPUTERS IN CLINICAL DEVELOPMENT 591

25. Clinical Data Collection and Management 593
Mazen Abdellatif

26. Regulation of Computer Systems 633
Sandy Weinberg

27. A New Paradigm for Analyzing Adverse Drug Events 649
Ana Szarfman, Jonathan G. Levine, and Joseph M. Tonning

PART VIII: FURTHER APPLICATIONS AND FUTURE DEVELOPMENT 677

28. Computers in Pharmaceutical Formulation 679
Raymond C. Rowe and Elizabeth A. Colbourn

29. Legal Protection of Innovative Uses of Computers in R&D 703
Robert Harrison

30. The Ethics of Computing in Pharmaceutical Research 715
Matthew K. McGowan and Richard J. McGowan

31. The UltraLink: An Expert System for Contextual Hyperlinking in Knowledge Management 729
Martin Romacker, Nicolas Grandjean, Pierre Parisot, Olivier Kreim, Daniel Cronenberger, Thérèse Vachon, and Manuel C. Peitsch

32. Powerful, Predictive, and Pervasive: The Future of Computers in the Pharmaceutical Industry 753
Nick Davies, Heather Ahlborn, and Stuart Henderson

INDEX 775